Yu, Misook

From: Yu, Misook
Sent: Tuesday, May 13, 2003 4:03 PM
To: Schreiber, David
Subject: 09654281

Would you please match SEQ ID NO:1 with NCBI accession numer P18031? Both should be proteins.

PTB-1B

Examiner Misook Yu, Ph.D.
703-308-2454 (Phone)
Art Unit 1642
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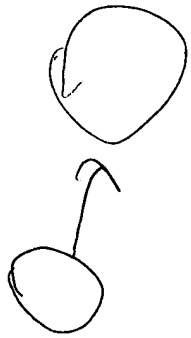
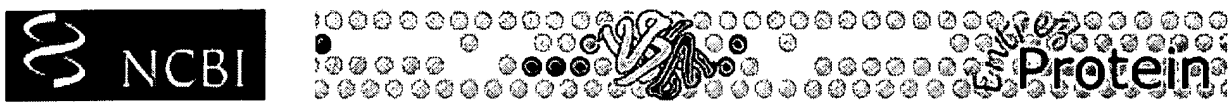


RKIP
Kinase
+
agent



☐ 1: P18031. Protein-tyrosine ...[gi:131467] BLink, Domains, Links

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ACCESSION P18031.
VERSION P18031 GI:131467
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extra accessions:Q9BQV9,Q9NQQ4,created: Nov 1, 1990.
sequence updated: Nov 1, 1990.
annotation updated: Sep 15, 2003.
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xrefs (non-sequence databases): GeneWHGNC:9642, MIM 176885, GO:GO:0007165, InterPro:IPR000387, InterPro:IPR000242, Pfam:PF00102, PRINTS:PR00700, SMART:SM00194, PROSITE:PS00383, PROSITE:PS50056, PROSITE:PS50055
KEYWORDS Hydrolase; Acetylation; Phosphorylation; 3D-structure.
SOURCE Homo sapiens (human)
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (residues 1 to 435)
AUTHORS Chernoff,J., Schievella,A.R., Jost,C.A., Erikson,R.L. and Neel,B.G.
TITLE Cloning of a cDNA for a major human protein-tyrosine-phosphatase
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 87 (7), 2735-2739 (1990)
MEDLINE 90207272
REMARK SEQUENCE FROM N.A.
TISSUE=Placenta
REFERENCE 2 (residues 1 to 435)
AUTHORS Brown-Shimer,S., Johnson,K.A., Lawrence,J.B., Johnson,C., Bruskin,A., Green,N.R. and Hill,D.E.
TITLE Molecular cloning and chromosome mapping of the human gene encoding protein phosphotyrosyl phosphatase 1B

JOURNAL Proc. Natl. Acad. Sci. U.S.A. 87 (13), 5148-5152 (1990)
MEDLINE 90311360
REMARK SEQUENCE FROM N.A.
TISSUE=Placenta
REFERENCE 3 (residues 1 to 435)
AUTHORS Deloukas,P., Matthews,L.H., Ashurst,J., Burton,J., Gilbert,J.G.R., Jones,M., Stavrides,G., Almeida,J.P., Babbage,A.K., Bagguley,C.L., Bailey,J., Barlow,K.F., Bates,K.N., Beard,L.M., Beare,D.M., Beasley,O.P., Bird,C.P., Blakey,S.E., Bridgeman,A.M., Brown,A.J., Buck,D., Burrill,W.D., Butler,A.P., Carder,C., Carter,N.P., Chapman,J.C., Clamp,M., Clark,G., Clark,L.N., Clark,S.Y., Clee,C.M., Clegg,S., Cobley,V.E., Collier,R.E., Connor,R.E., Corby,N.R., Coulson,A., Coville,G.J., Deadman,R., Dhami,P.D., Dunn,M., Ellington,A.G., Frankland,J.A., Fraser,A., French,L., Garner,P., Grafham,D.V., Griffiths,C., Griffiths,M.N.D., Gwilliam,R., Hall,R.E., Hammond,S., Harley,J.L., Heath,P.D., Ho,S., Holden,J.L., Howden,P.J., Huckle,E., Hunt,A.R., Hunt,S.E., Jekosch,K., Johnson,C.M., Johnson,D., Kay,M.P., Kimberley,A.M., King,A., Knights,A., Laird,G.K., Lawlor,S., Lehvaeslaiho,M.H., Leversha,M.A., Lloyd,C., Lloyd,D.M., Lovell,J.D., Marsh,V.L., Martin,S.L., McConnachie,L.J., McLay,K., McMurray,A.A., Milne,S.A., Mistry,D., Moore,M.J.F., Mullikin,J.C., Nickerson,T., Oliver,K., Parker,A., Patel,R., Pearce,T.A.V., Peck,A.I., Phillimore,B.J.C.T., Prathalingam,S.R., Plumb,R.W., Ramsay,H., Rice,C.M., Ross,M.T., Scott,C.E., Sehra,H.K., Shownkeen,R., Sims,S., Skuce,C.D., Smith,M.L., Soderlund,C., Steward,C.A., Sulston,J.E., Swann,R.M., Sycamore,N., Taylor,R., Tee,L., Thomas,D.W., Thorpe,A., Tracey,A., Tromans,A.C., Vaudin,M., Wall,M., Wallis,J.M., Whitehead,S.L., Whittaker,P., Willey,D.L., Williams,L., Williams,S.A., Wilming,L., Wray,P.W., Hubbard,T., Durbin,R.M., Bentley,D.R., Beck,S. and Rogers,J.
TITLE The DNA sequence and comparative analysis of human chromosome 20
JOURNAL Nature 414 (6866), 865-871 (2001)
MEDLINE 21638749
REMARK SEQUENCE FROM N.A.
REFERENCE 4 (residues 1 to 435)
AUTHORS Strausberg,R.L., Feingold,E.A., Grouse,L.H., Derge,J.G., Klausner,R.D., Collins,F.S., Wagner,L., Shenmen,C.M., Schuler,G.D., Altschul,S.F., Zeeberg,B., Buetow,K.H., Schaefer,C.F., Bhat,N.K., Hopkins,R.F., Jordan,H., Moore,T., Max,S.I., Wang,J., Hsieh,F., Diatchenko,L., Marusina,K., Farmer,A.A., Rubin,G.M., Hong,L., Stapleton,M., Soares,M.B., Bonaldo,M.F., Casavant,T.L., Scheetz,T.E., Brownstein,M.J., Usdin,T.B., Toshiyuki,S., Carninci,P., Prange,C., Raha,S.S., Loquellano,N.A., Peters,G.J., Abramson,R.D., Mullahy,S.J., Bosak,S.A., McEwan,P.J., McKernan,K.J., Malek,J.A., Gunaratne,P.H., Richards,S., Worley,K.C., Hale,S., Garcia,A.M., Gay,L.J., Hulyk,S.W., Villalon,D.K., Muzny,D.M., Sodergren,E.J., Lu,X., Gibbs,R.A., Fahey,J., Helton,E., Ketteman,M., Madan,A., Rodrigues,S., Sanchez,A., Whiting,M., Madan,A., Young,A.C., Shevchenko,Y., Bouffard,G.G., Blakesley,R.W., Touchman,J.W., Green,E.D., Dickson,M.C., Rodriguez,A.C., Grimwood,J., Schmutz,J., Myers,R.M., Butterfield,Y.S.N., Krzywinski,M.I., Skalska,U., Smailus,D.E., Schnerch,A., Schein,J.E., Jones,S.J.M. and Marra,M.A.
TITLE Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 99 (26), 16899-16903 (2002)
MEDLINE 22388257
REMARK SEQUENCE FROM N.A.

TISSUE=Eye, and Lymph
REFERENCE 5 (residues 1 to 435)
AUTHORS Charbonneau,H., Tonks,N.K., Kumar,S., Diltz,C.D., Harrylock,M., Cool,D.E., Krebs,E.G., Fischer,E.H. and Walsh,K.A.
TITLE Human placenta protein-tyrosine-phosphatase: amino acid sequence and relationship to a family of receptor-like proteins
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 86 (14), 5252-5256 (1989)
MEDLINE 89315775
REMARK SEQUENCE OF 1-321.
TISSUE=Placenta
REFERENCE 6 (residues 1 to 435)
AUTHORS Flint,A.J., Gebbink,M.F., Franza,B.R. Jr., Hill,D.E. and Tonks,N.K.
TITLE Multi-site phosphorylation of the protein tyrosine phosphatase, PTP1B: identification of cell cycle regulated and phorbol ester stimulated sites of phosphorylation
JOURNAL EMBO J. 12 (5), 1937-1946 (1993)
MEDLINE 93259136
REMARK PHOSPHORYLATION SITES.
REFERENCE 7 (residues 1 to 435)
AUTHORS Frangioni,J.V., Beahm,P.H., Shifrin,V., Jost,C.A. and Neel,B.G.
TITLE The nontransmembrane tyrosine phosphatase PTP-1B localizes to the endoplasmic reticulum via its 35 amino acid C-terminal sequence
JOURNAL Cell 68 (3), 545-560 (1992)
MEDLINE 92154669
REMARK SUBCELLULAR LOCATION.
REFERENCE 8 (residues 1 to 435)
AUTHORS Barford,D., Flint,A.J. and Tonks,N.K.
TITLE Crystal structure of human protein tyrosine phosphatase 1B
JOURNAL Science 263 (5152), 1397-1404 (1994)
MEDLINE 94174273
REMARK X-RAY CRYSTALLOGRAPHY (2.8 ANGSTROMS) OF 1-321.
REFERENCE 9 (residues 1 to 435)
AUTHORS Puius,Y.A., Zhao,Y., Sullivan,M., Lawrence,D.S., Almo,S.C. and Zhang,Z.Y.
TITLE Identification of a second aryl phosphate-binding site in protein-tyrosine phosphatase 1B: a paradigm for inhibitor design
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 94 (25), 13420-13425 (1997)
MEDLINE 98054248
REMARK X-RAY CRYSTALLOGRAPHY (1.9 ANGSTROMS) OF 1-298 OF MUTANT SER-215.
REFERENCE 10 (residues 1 to 435)
AUTHORS Pannifer,A.D., Flint,A.J., Tonks,N.K. and Barford,D.
TITLE Visualization of the cysteinyl-phosphate intermediate of a protein-tyrosine phosphatase by x-ray crystallography
JOURNAL J. Biol. Chem. 273 (17), 10454-10462 (1998)
MEDLINE 98221181
REMARK X-RAY CRYSTALLOGRAPHY (2.5 ANGSTROMS) OF 1-285.
REFERENCE 11 (residues 1 to 435)
AUTHORS Groves,M.R., Yao,Z.J., Roller,P.P., Burke,T.R. Jr. and Barford,D.
TITLE Structural basis for inhibition of the protein tyrosine phosphatase 1B by phosphotyrosine peptide mimetics
JOURNAL Biochemistry 37 (51), 17773-17783 (1998)
MEDLINE 99119205
REMARK X-RAY CRYSTALLOGRAPHY (2.35 ANGSTROMS) OF 1-298.
COMMENT ----------

[CATALYTIC ACTIVITY] Protein tyrosine phosphate + H(2)0 = protein tyrosine + phosphate.
[SUBCELLULAR LOCATION] ASSOCIATED TO THE ENDOPLASMIC RETICULUM VIA ITS C-TERMINAL DOMAIN WITH ITS PHOSPHATASE DOMAIN ORIENTED TOWARDS THE CYTOPLASM.
[SIMILARITY] BELONGS TO THE NON-RECEPTOR CLASS OF THE PROTEIN-TYROSINE PHOSPHATASE FAMILY.

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Region	40..288 /gene="PTPN1" /region_name="Domain" /note="PROTEIN-TYROSINE PHOSPHATASE."
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May 2 2003 16:47:12

***604591** Links

PHOSPHATIDYLETHANOLAMINE-BINDING PROTEIN; PBP

Alternative titles; symbols

RAF KINASE INHIBITOR PROTEIN
RKIP HIPPOCAMPAL CHOLINERGIC NEUROSTIMULATING PEPTIDE PRECURSOR PROTEIN
HCNP PRECURSOR PROTEIN

Gene map locus Chr.12

TEXT

CLONING

Yeung et al. (1999) used a yeast 2-hybrid screen to identify RAF1 (164760)-interacting proteins. They identified a protein, designated RKIP (RAF kinase inhibitor protein), that inhibits the phosphorylation and activation of MEK (176872) by RAF1. MEK is a kinase that activates the extracellular signal-regulated kinases (ERKs; see 176872). This kinase cascade controls the proliferation and differentiation of different cell types. RKIP is identical to the phosphatidylethanolamine-binding protein (PBP) with a relative molecular mass 23 kD.

Seddiqi et al. (1994) determined that the human RKIP cDNA encodes a protein of 186 amino acids, the sequence of which is 95% identical to the bovine 21- to 23-kD protein. The rat protein shows 85.5% identity with the human protein. Schoentgen and Jolles (1995) demonstrated that the bovine protein was highly expressed in the brain and associated with cytosolic proteins and small GTP-binding proteins. Multiple tissue Northern blots revealed the presence of a single mRNA in the different tissues of each species; a single band of 1.8 kb was identified in human, 1.45 kb in mouse, and 1.2 kb in rat tissues. The mRNA is particularly highly expressed in rat and mouse testis, where the level was 30 times higher than that in the brain. The mRNA was not observed in human testis by Northern blot analysis, and was detected only by PCR.

Tohdoh et al. (1995) cloned phosphatidylethanolamine-binding protein, which they called the hippocampal cholinergic neurostimulating peptide, or HCNP, precursor protein. Hori et al. (1994) sequenced about 1,000 3-prime-directed cDNA clones from

the human HepG2 cell line and found that 1 of the cDNAs encoded the human homolog of bovine PBP. They found that the cDNA consists of 1,434 nucleotides with a 91-nucleotide 5-prime noncoding sequence followed by a 187-amino acid coding region and a 779-nucleotide 3-prime noncoding sequence. Moore et al. (1996) cloned the brain phosphatidylethanolamine-binding protein and found it to be identical in sequence to the protein cloned by Hori et al. (1994). Moore et al. (1996) used polyclonal antibodies in immunohistochemical studies in brain tissue and found that PBP is expressed strongly in the cell bodies of oligodendrocytes but only weakly elsewhere. Schwann cells and spinal nerve roots showed intense cytoplasmic PBP immunoreactivity.

GENE FUNCTION

Yeung et al. (1999) demonstrated that, in vitro, RKIP binds to RAF1, MEK, and ERK, but not to RAS (190020). RKIP coimmunoprecipitates with RAF1 and MEK from cell lysates and colocalizes with RAF1 when examined by confocal microscopy. RKIP is not a substrate for RAF1 or MEK but competitively disrupts the interaction between these kinases. RKIP overexpression interferes with the activation of MEK and ERK, induction of AP1 (165160)-dependent reporter genes, and transformation elicited by an oncogenically activated RAF1 kinase. Downregulation of endogenous RKIP by expression of antisense RNA or antibody microinjection induces the activation of MEK-, ERK-, and AP1-dependent transcription. Yeung et al. (1999) concluded that RKIP represents a class of protein kinase inhibitor protein that regulates the activity of the Raf/MEK/ERK module.

Hengst et al. (2001) determined that the residual thrombin (176930) inhibitory activity in the brains of nexin (PI7; 177010)-null mice was due to Pbp. By coimmunoprecipitation and mobility shift assays, they demonstrated direct binding between recombinant human thrombin and Pbp in mouse brain lysates. By in vitro assay of PBP against several serine proteases, they determined that PBP is a competitive inhibitor of thrombin and chymotrypsin (see CTRB1, 118890) but not of trypsin, tissue plasminogen activator, or pancreatic elastase. Hengst et al. (2001) also detected Pbp immunostaining on the extracellular surface of transfected cells as well as in the conditioned medium.

MAPPING

The International Radiation Hybrid Mapping Consortium mapped the PBP gene to chromosome 12 (RH26435).

REFERENCES

1. Hengst, U.; Albrecht, H.; Hess, D.; Monard, D. :
The phosphatidylethanolamine-binding protein is the prototype of a novel family of serine protease inhibitors. *J. Biol. Chem.* 276: 535-540, 2001.
PubMed ID : 11034991

2. Hori, N.; Chae, K.; Murakawa, K.; Matoba, R.; Fukushima, A.; Okubo, K.; Matsubara,

K. :
A human cDNA sequence homologue of bovine phosphatidylethanolamine-binding protein. *Gene* 140: 293-294, 1994.
PubMed ID : 8144042

3. Moore, C.; Perry, A. C. F.; Love, S.; Hall, L. :
Sequence analysis and immunolocalisation of phosphatidylethanolamine binding protein (PBP) in human brain tissue. *Molec. Brain Res.* 37: 74-78, 1996.
PubMed ID : 8738137

4. Schoentgen, F.; Jolles, P. :
From structure to function: possible biological roles of a new widespread protein family binding hydrophobic ligands and displaying a nucleotide binding site. *FEBS Lett.* 369: 22-26, 1995.
PubMed ID : 7641877

5. Seddiqi, N.; Bollengier, F.; Alliel, P. M.; Perin, J.-P.; Bonnet, F.; Bucquoy, S.; Jolles, P.; Schoentgen, F. :
Amino acid sequence of the Homo sapiens brain 21-23-kDa protein (neuropolypeptide h3), comparison with its counterparts from Rattus norvegicus and Bos tauras species, and expression of its mRNA in different tissues. *J. Molec. Evol.* 39: 655-660, 1994.
PubMed ID : 7807553

6. Tohdoh, N.; Tojo, S.; Agui, H.; Ojika, K. :
Sequence homology of rat and human HCNP precursor proteins, bovine phosphatidylethanolamine-binding protein and rat 23-kDa protein associated with the opioid-binding protein. *Molec. Brain Res.* 30: 381-384, 1995.
PubMed ID : 7637590

7. Yeung, K.; Seitz, T.; Li, S.; Janosch, P.; McFerran, B.; Kaiser, C.; Fee, F.; Katsanakis, K. D.; Rose, D. W.; Mischak, H.; Sedivy, J. M.; Kolch, W. :
Suppression of Raf-1 kinase activity and MAP kinase signalling by RKIP. *Nature* 401: 173-177, 1999.
PubMed ID : 10490027

CONTRIBUTORS

Patricia A. Hartz - updated : 7/9/2002
Ada Hamosh - updated : 2/24/2000

CREATION DATE

Ada Hamosh : 2/22/2000

EDIT HISTORY

carol : 7/9/2002

terry : 10/4/2000
alopez : 3/3/2000
alopez : 3/2/2000
terry : 2/24/2000
alopez : 2/23/2000
alopez : 2/22/2000

WEST

09/654,281 Case Creation Option

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Q2	Q1 and rkip	USPT	ASSIGNEE	ADJ	YES
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Q4	Q3 and (mapk or erk)	USPT	ASSIGNEE	ADJ	YES
Q5	Q4 and inhibit$3	USPT	ASSIGNEE	ADJ	YES
Q6	inhibitor$1 raf-1	USPT	None	ADJ	YES
Q7	raf inhibitor@1	USPT	None	ADJ	YES
Q8	raf inhibitor$1	USPT	None	ADJ	YES
Q9	inhibit raf kinase	USPT	None	ADJ	YES

Overwrite Cancel

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